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Administration of Intranasal Insulin During Cardiopulmonary Resuscitation Improves Neurological Outcomes After Cardiac Arrest

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INTRODUCTION: Over 325,000 people die from cardiac arrest each year. Prognosis is poor and survivors typically experience persistent neurologic deficits. Currently, neuroprotective treatments to reduce brain injury in cardiac arrest survivors are limited and ineffective. This study evaluates the potential neuroprotection induced by high dose intranasal insulin (HD-IN-I) in a rodent model of asphyxial cardiac arrest.

METHODS: Male Long Evans rats were block randomized to sham-operated controls or 8-minute asphyxial cardiac arrest treated with placebo or HD-IN-I at the onset of CPR. To investigate mechanism of action, hippocampi were collected 30 minutes post-ROSC and analyzed by Western blot for phosphorylation of Akt. To assess long-term functional outcomes, neurobehavioral evaluation was conducted using neurologic function scores daily and Barnes maze, Rotarod, and passive avoidance on days 7-10 post-ROSC. Histologic quantification of surviving hippocampal CA1 pyramidal neurons was also conducted.

RESULTS: Hippocampal phospho-Akt/total Akt ratio increased 2-fold in the placebo group and 5.7-fold in HD-IN-I group relative to shams ($p < 0.05$). Rats treated with HD-IN-I had significantly improved performance on Rotarod, Barnes maze, and passive avoidance ($p < 0.05$). HD-IN-I had no significant effect on ROSC rate, 10-day survival, systemic glycemic response, or on the number of surviving CA1 pyramidal neurons compared to placebo treatment.

DISCUSSION: This study is the first to demonstrate that HD-IN-I administered at the onset of CPR, causes phosphorylation of brain Akt and results in significant neuroprotection. This primary work strongly suggests that intranasal insulin could be the first highly effective neuroprotective treatment for cardiac arrest patients.